85

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,500	11/29/2000	David A Cheresh	TSRI 651.1	5356

2387 7590 11/03/2004

OLSON & HIERL, LTD.
20 NORTH WACKER DRIVE
36TH FLOOR
CHICAGO, IL 60606

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,500	CHERESH ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,14-16,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,14-16,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/04 has been entered.

An amendment after final was received on 6/23/04, but was not entered at that time. This amendment was entered with the filing of the RCE on 10/5/04.

Claims 1, 4, 14-16, 33, and 34 are pending and under consideration in this Office Action.

Specification

The specification is objected to. At page 4 the brief description of Fig. 7 describes Figures 7A and 7B, however, Fig. 7 does not contain Figures 7A and 7B.

Claim Objections

Claim 16 is objected to because it recites "an non-viral". Substitution of "a" for "an" is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 1, 4, 14-16, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 4, 14-16, 33, and 34 have been amended to require "an amount of a nucleic acid sufficient to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition." In the response filed 6/23/04 Applicant states that support for amendments can be found at page 25, line 28 through page 26, line 19; page 26, lines 23-31, and page 27, lines 1-27. From these passages, the following excerpt at page 26, lines 23-31 is pertinent:

> A therapeutic composition contains an angiogenesis-modulating amount of an Src protein of the present invention, or sufficient recombinant DNA expression vector to express an effective amount of Src protein, typically formulated to contain an amount of at least 0.1 weight percent of Src protein per weight of total therapeutic composition. A weight percent is a ratio by weight of Src protein to total composition. Thus. for example, 0.1 weight percent is 0.1 grams of Src protein per 100 grams of total composition. For DNA expression vectors, the amount administered depends on the properties of the expression vector, the tissue to be treated, and the like considerations.

The first sentence of this passage relates to the amount of Src protein that is present in a therapeutic composition, and mentions as an alternative that a therapeutic

composition may contain "sufficient recombinant DNA expression vector to express an effective amount of Src protein." The clause "typically formulated to contain an amount of at least 0.1 weight percent of Src protein per weight of total therapeutic composition" cannot logically apply to the clause regarding the DNA expression vector because it describes a composition that comprises protein, not an expression vector. This phrase describes only the proportion of protein in a total formulation, and has no bearing on what is an "angiogenesis-modulating amount" or "an effective amount" of Src protein. There is no nexus between the amount of expression vector required to express an effective amount of Src protein and the *proportion* of Src protein in any therapeutic composition. Also, the passage does not take into account the difference between "comprising" and "delivering". In practice, delivery to cells is never 100% efficient, and some portion of the administered drug is generally eliminated from the organism without having been delivered. In the case of a nucleic acid drug, in order to deliver a protein the nucleic acid must successfully enter a cell and be expressed. The passage relied upon for support simply does not address the amount of a nucleic acid that is required to *deliver* 0.1 weight percent of Src protein per weight of total therapeutic composition. It concerns only the proportion of protein in a therapeutic composition. As a result the claims contain new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al (FEBS Lett. 411:317-321, 1997), as evidenced by the instruction manual for the BioRad Gene Pulser, retrieved on 10/15/2004 from http://researchlink.labvelocity.com/protocols/protocol.jhtml?sourceId=25&path=0%7C669%7C1014%7C848&nodeId=848&id=2121.

Kato teaches a non-viral vector (pOPI3) comprising a human c-Src cDNA, and the use of the vector to transfect NIH 3T3 cells by electroporation using a BioRad Gene Pulser apparatus. As is apparent to one of ordinary skill in the art, in order to work with nucleic acid compositions, the compositions must be contained somehow, e.g. in a vial, a microfuge tube, a pipette tip, or even an electroporation cuvette. The operating instructions for the electroporation apparatus used by Kato show that the electroporation process involves placing the nucleic acid into an article of manufacture, i.e. an electroporation cuvette. See e.g. page 12, item 4. It is clear that the nucleic acid of Kato was in a carrier/excipient i.e. water, because the electroporation procedure is carried out with nucleic acids in a cell suspension. See e.g. page 12, item 4, or page 14, last full paragraph of the instruction manual.

It is noted that, in order to be enabled, the claimed composition must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The claims as amended also require an amount of the nucleic acid sufficient to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. The instant

specification provides no guidance as to what is the minimum amount of the composition which is required to stimulate angiogenesis, or what amount of nucleic acid will to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. Because the claimed pharmaceutical composition and the composition of Kato are structurally indistinguishable, the composition of Kato is considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus Kato anticipates the claims.

Claims 1, 4, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanaka et al (Mol. Cell. Biol. 6(11): 3900-3909, 1986). This is a new ground of rejection.

Tanaka teaches isolation of a retroviral vector (WO CS) encoding a human c-src protein. See entire document, especially abstract. It is readily apparent to one of ordinary skill in the art, in order to isolate virus vectors, the vectors must be contained somehow, in an article of manufacture, e.g. in a vial, or microfuge tube. Thus Tanaka anticipates the claims.

Response to Arguments

Applicants arguments filed 6/23/04 have been considered as the may apply to the grounds of rejection set forth above, but are unpersuasive.

Applicant addresses the anticipation rejections at pages 4-7 of the response. Applicant notes at page 5 that claims 1, 4, and 14-16 are drawn to articles of manufacture, and argues that the cited art does not teach an article of manufacture comprising packaging material. This is unpersuasive because it is clear that one cannot work with nucleic acids or virus vectors in the manner disclosed in the cited art without the aid of packaging materials such as vials, microfuge tubes, pipette tips or electroporation cuvettes that are used to contain the nucleic acids or viral vectors. Further, as discussed more fully below, the claimed nucleic acid is the functional element of the invention, and the recited packaging material is not functionally related to the recited nucleic acid. The packaging material in no way affects the structure or function of the nucleic acid. As a result, the packaging material will not distinguish the claimed nucleic acid from the nucleic acid of the prior art.

At pages 5-7 of the response, Applicant argues the significance of printed words on a label. Applicant argues that the instant situation is analogous to those in *In re Mi*ller and *In re Gulack* because the claimed printed instructions change the intrinsic quality of the article by imparting a new functionality to the article. This argument is unpersuasive because the situations are not analogous. The functional element of the invention is the nucleic acid that encodes the human src protein and can stimulate angiogenesis. The packaging material cannot stimulate angiogenesis. The label cannot stimulate angiogenesis. The situations are not analogous because neither the packaging material nor the printed instructions change the functionality of the nucleic acid in any way. The nucleic acid still encodes the same protein known in the prior art, and the protein still catalyzes the same kinase reaction known in the prior art. The activity of this kinase is required for the stimulation of angiogenesis. The presence of packaging material or instructions changes nothing with regard to the intrinsic function of the nucleic acid. In contrast, in both *Gulack* and *Miller*, the printed matter changed the intrinsic qualities of the material to which it was applied. In other words, the functions of the claimed devices depended on the printed matter itself, which was part of the substrate. That is, the printed matter was part of the hat in *Gulack*, and part of the cup in *Miller,* and in each case the printed matter altered both the structure and the function of the material to which it was applied. In both cases, without the printed material, the substrates lose their function. In the instant case, the printed matter is merely a label that indicates that the claimed nucleic acid may be used for a particular purpose, but the label itself does not change the structure of the claimed nucleic acid or

confer any new or different functionality on the claimed nucleic acid. In fact, the nucleic acid retains its full functionality absent the recited printed material.

Applicant's argument is based on the premise that the claimed label changes the intrinsic quality of the article by imparting a new functionality to the article. This argument is unpersuasive because the label does not change in any way the intrinsic nature of the nucleic acid, i.e. its structure or its function. Instead, the label merely describes a new use for an old product. This situation was considered by the court recently in *In re Ngai* (70 USPQ2D 1862). A claim directed to a kit for performing a method of normalizing and amplifying ribonucleic acids was properly rejected as anticipated by the prior art, even though the content of instructions in the claimed kit differed from instructions in the prior art. In the decision, the court depended on the findings in *In re Gulack* and found that "addition of a new set of instructions into a known kit does not interrelate with the kit in the same way as the numbers interrelated with the band. In Gulack, the printed matter would not achieve its educational purposes without the band, and the band without the printed matter would similarly be unable to produce the desired result. Here, the printed matter in no way depends on the kit, and the kit does not depend on the printed matter. *All that the printed matter does is teach a new use for an existing product."* Emphasis added. The instant situation is similar in that the nucleic acid will function identically in the presence or absence of the claimed label. It will encode the same protein with the same structure and function. The label merely refers to a new use for the old product. The court in *Ngai* went on to say that "[a]s the Gulack court pointed out, "[w]here the printed matter is not functionally related

to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." Id. If we were to adopt Ngai's position, anyone could continue patenting a product indefinitely provided that they add a new instruction sheet to the product. This was not envisioned by Gulack." In the instant case, neither the packaging material nor the printed matter is functionally related to the nucleic acid, so neither one will patentably distinguish the invention from the nucleic acid of the prior art.

For these reasons the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al (FEBS Lett. 411:317-321, 1997), in view of Boyse et al (US Patent 5,004,861, issued 4/2/1991).

Kato teaches a method in which expression vectors comprising a human c-Src cDNA are used to stably transfect cultured cells for the purpose of studying cellular metabolism. The cells were transfected by electroporation.

Kato does not teach a liposome or a viral vector.

Boyse teaches methods of making stably transfected cells with genes. At paragraph 148 of the detailed description, Boyse notes that numerous techniques are known in the art for the stable introduction of foreign genes into cells, and further states:

> Techniques which may be used include but are not limited to chromosome transfer (e.g., cell fusion, chromosome-mediated gene transfer, micro cell-mediated gene transfer), physical methods (e.g., transfection, spheroplast fusion, microinjection, electroporation, liposome carrier), viral vector transfer (e.g., recombinant DNA viruses, recombinant RNA viruses) etc. [citation omitted].

Thus Boyse teaches that electroporation, liposome-mediated transfection, and virus-mediated transfection are interchangeable for the purpose of delivering genes to cells. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). For these reasons it would have been obvious to one of ordinary skill in the art at the time of the invention to use liposomes to transfer into cells the human c-src expression vector of Kato. Similarly, it would have been obvious to construct and use a viral vector comprising the human c-Src cDNA. Regarding the claimed packaging material, it is readily apparent to one of ordinary skill in the art that in order to work with nucleic acid compositions, the compositions must be contained somehow, e.g. in a vial, a microfuge tube, or a pipette tip. As such the presence of a packaging material is considered to be obvious, and the invention as a whole was prima facie obvious.

It is noted that, in order to be enabled, the claimed composition must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The claims as

amended also require an amount of the nucleic acid sufficient to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. The instant specification provides no guidance as to what is the minimum amount of the composition which is required to stimulate angiogenesis, or what amount of nucleic acid will to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. Because the claimed pharmaceutical composition and the composition of Kato are structurally indistinguishable, the composition of Kato is considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 33 and 34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al (FEBS Lett. 411:317-321, 1997), in view of Boyse et al (US Patent 5,004,681, issued 4/2/1991) and GenBank Accession No. X59932.

The teachings of Boyse and Kato are summarized above, and render obvious compositions comprising a human c-Src expression vector associated with liposomes, and a viral expression vector encoding human c-Src.

Kato is silent as to the sequence of the human c-src encoded by the cDNA.

GenBank Accession No. X59932 teaches a nucleic acid encoding a human c-Src polypeptide having the sequence of SEQ ID NO:5.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use in the invention of Kato the c-Src sequence disclosed in GenBank Accession No. X59932. The essential feature of the cDNA of Kato is that it encoded a human c-SRC with kinase activity. The nucleic acid of GenBank Accession No. X59932 encodes a human c-Src kinase. As such, these nucleic acids would be considered by those of ordinary skill in the art to be interchangeable in the invention of Kato, and so they are equivalents. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known

material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

It is noted that, in order to be enabled, the claimed composition must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The claims as amended also require an amount of the nucleic acid sufficient to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. The instant specification provides no guidance as to what is the minimum amount of the composition which is required to stimulate angiogenesis, or what amount of nucleic acid will to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical composition. Because the claimed pharmaceutical composition and the composition of Kato are structurally indistinguishable, the composition of Kato is considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195

USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicants arguments filed 6/23/04 have been considered as the may apply to the grounds of rejection set forth above, but are unpersuasive.

Applicant argues at pages 7 and 8 of the response that Kato does not teach several limitations of the claims, as discussed in the response to the rejections under 35 USC 102, and that the secondary references also fail to teach these limitations. Applicant's arguments regarding the Kato reference are unpersuasive for the reasons given above under 35 USC 102 rejections. Applicant has not argued that the secondary references do not teach the limitations for which they were relied upon. For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.